REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

At the outset, the undersigned again wishes to express appreciation to the Examiner for granting the interview of January 13, 2005. The Examiner's Summary accurately reflects the substance of that interview. Accordingly, no further comment is believed necessary.

Claim 19 has been cancelled without prejudice. Claim 39 has been revised to define the invention with additional clarity. Specifically, claim 39 has been revised so as to be drawn to a method of stimulating cytotoxic T lymphocyte proliferation rather than to a method of producing cytotoxic T lymphocytes. Support for the amendment to claim 39 is found, for example, at page 4, line 28 to page 5, line 5, taken with page 13, lines 4-9.

New dependent claims 40 and 42 do not raise any new issue as they each recite one of the two options provided for in claim 39 (that is, tumor-derived RNA in the case of claim 40 and pathogen-derived RNA in the case of claim 42). Similarly, new dependent claims 41 and 43 do not raise any new issue as they each recite one of the two options provided for in now cancelled claim 19 (that is, tumor-specific RNA in the case of claim 41 and pathogen-specific RNA in the case of claim 43) (page 2, lines 15-20, and page 6, lines 4-26, make it clear that tumor- and pathogen-derived RNA includes tumor- and pathogen-specific RNA, respectively). New claim 44 depends from claim 39 and

indicates that the CTL cultured in step (iii) are able to lyse a target cell. Pathogen cells and pathogen infected cells are included within the meaning of "target cell". For example, page 1, lines 26-32 recite: "A variety of methods have been described for treating infections with intracellular pathogens such as viruses and bacteria. . . CTL-based therapies have been described for treating such infection"(underlining added). Page 27, lines 11-17, recites: "the invention can be used to treat or prevent infection in a patient with a pathogen such as a bacterium (e.g., *Salmonella*, *Shigella*, or *Enterobacter*) or a virus (e.g., a human immunodeficiency virus, a Herpes virus, an influenza virus, a poliomylelitis virus, a measles virus, a mumps virus, or a rubella virus)." Page 6, lines 9-11 give as examples of a pathogen "e.g., a bacterium or virus, including intracellular pathogens". Accordingly, one of skill in the art would recognize that "target cell" encompasses tumor cells, pathogen cells (e.g., bacteria or other cellular pathogens) and cells containing intracellular pathogens (e.g., viruses and other intracellular pathogens).

New claim 45 is drawn to a method of producing a CTL (support for "producing a CTL" can be found, for example, at page 4, lines 28-29). This new claim is not believed to raise any new issues. Step (i) of this method is identical to step (i) of claim 39. Step (ii) of this method reads differently than step (ii) of claim 39 in that in claim 45, the APC produced in the preceding step is contacted with a $CD8^+$ T cell, thereby producing a CTL from the $CD8^+$ T cell. In claim 39, the APC are contacted with lymphocytes comprising CTL, thereby producing CTL that recognize the antigen. As the Examiner likely knows,

CD8+ T cells function as CTL (see page 22, line 6 to page 23, line 5). New claims 46-50 depend from claim 45 and parallel the language of claims 40-44, respectively.

Turning now to the Examiner's specific concerns, it is noted that claim 19 stands rejected under 35 USC 112, first paragraph. Withdrawal of the rejection is submitted to be in order in view of the cancellation of claim 19. The rejection is not believed to be applicable to the newly presented claims for the reasons that follow.

New claims 41, 43, 47, 49, like now cancelled claim 19, make reference to tumor-specific or pathogen-specific RNA. The Examiner previously contended that the specification does not teach how to separate RNA that is specific to pathogens or tumors from non-specific RNA. From the Advisory Action, it is clear that the Examiner now appreciates that the application specifically teaches at least one method by which such separations can be performed:

> tumor-specific RNA can be prepared by fractionating tumor-derived RNA using **conventional** subtractive hybridization techniques against RNA from non-tumor cells. Likewise, "pathogen-specific" RNA refers to an RNA sample that, relative to unfractionated pathogen-derived RNA, has a high content of RNA that is preferentially present in the pathogen compared with a non-pathogenic strain of bacteria or virus.

(See page 7, lines 13-20, emphasis added.)

That subtractive hybridization was a conventional technique in the art as of the earliest priority date of the application, April 30, 1996, will be apparent from the following references (further copies of which are attached – these documents are listed on the attached PTO 1449 Form which the Examiner is again requested to initial and return as the prior Amendment was not entered):

i) Molecular Biology of the Cell, 3rd Ed. (1994) Alberts, et al., (Ed.) Garland Publishing, Inc, New York, NY, page 312, especially figure 7-25.

ii) U.S. 5,256,536 (issued 26 October 1993), Example 1.

As the Examiner appreciates, while subtractive hybridization could be used, other techniques could also be applied.

In view of the above, it will be clear that preparing tumor- or pathogen-specific RNA would not have required undue experimentation.

At the time of the interview, the undersigned discussed with the Examiner a number of documents predating the effective filing date of the instant application and relating to a variety of "tumor-specific" antigens/encoding sequences. Pursuant to the Examiner's request, copies of those documents were submitted January 13, 2005, further copies are submitted herewith in view of the fact that the January 13, 2005 was not entered (they are also listed on the attached PTO 1449 Form which the Examiner is, again, requested to initial and return). The documents make clear the art-recognized scope of the term "tumor-specific".

The Examiner is respectfully requested to again acknowledge withdrawal of the rejection under 35 USC 112, first paragraph.

Claims 19 and 39 stand rejection as allegedly representing obviousness-type double patenting over claims 1-14 of USP 6,670,186 in view of the disclosure of '186. Claims 19 and 39 also stand rejected as allegedly representing obviousness-type double patenting over claims 1-8 of USP 6,387,701 in view of the disclosure of '701.

Additionally, claims 19 and 39 stand rejected as allegedly representing obviousness-type double patenting over claims 1-29 of USP 6,306,388 in view of the disclosure of '388. While in no way agreeing with the Examiner's assertions, submitted herewith are further copies of Terminal Disclaimers that moot the rejections (as the required fee was submitted with the Amendment filed January 13, 2005, no further fee is believed necessary but should the Office take a different view, authorization is hereby give to debit the undersigned firm's account (account no. 14-1140)).

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

NAIR et al

Atty. Ref.: 1579-579

Serial No. 09/875,264

TC/A.U.: 1632

Filed: June 7, 2001

Examiner: Wilson, M.

For: METHODS FOR TREATING CANCERS AND PATHOGEN INFECTIONS USING ANTIGEN-PRESENTING CELLS LOADED WITH RNA

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

TERMINAL DISCLAIMER

Your petitioner, DUKE UNIVERSITY, a corporation having an office and place of business at Durham, North Carolina 27710 represents that it is the assignee as recorded in an assignment at Reel 8080/Frame 0488, of all right, title and interest in and to Application Serial No. 09/875,264, filed June 7, 2001, for METHODS FOR TREATING CANCERS AND PATHOGEN INFECTIONS USING ANTIGEN-PRESENTING CELLS LOADED WITH RNA.

Your petitioner hereby disclaims the terminal part of any patent granted on the above-identified application, which would extend beyond the expiration date of the full statutory term as presently shortened by any terminal disclaimer of Patent No. 6,670,186 and hereby agrees that any patent so granted on the above-identified application shall be enforceable only for and during such period that the legal title to such patent granted on

the above-identified application shall be the same as the legal title to the above-identified Patent No. 6,670,186, this agreement to run with any patent granted on the above-identified application and to be binding upon the grantee, its successors or assigns.

Petitioner does not disclaim any terminal part of any patent granted on the above-identified application prior to the expiration date of the full statutory term as presently shortened by any terminal disclaimer of Patent No. 6,670,186 in the event that it later: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321(a), has all claims canceled by a reexamination certificate, or is otherwise terminated prior to the expiration of its statutory term as presently shortened by any terminal disclaimer, except for the separation of legal title stated above.

The evidentiary documents accompanying this document or referred to above have been reviewed by the undersigned and it is certified that to the best of the assignee's knowledge and belief, title is in the assignee seeking to take action.

Check either box 1 or 2 below, as appropriate.

1. ☒ For submissions on behalf of an organization (e.g., corporation, partnership, university, government agency, etc.), the undersigned is empowered to act on behalf of the organization.

2. ☐ The undersigned is an attorney or agent of record.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the

like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

DUKE UNIVERSITY

By: _____

Name: Robert L. Taber
Title: Vice Chancellor, Science & Technology Development

Date: November 9, 2004

☒ **Terminal disclaimer fee under 37 C.F.R. § 1.20(d) included.** If missing, the Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140. A duplicate copy of this sheet is attached.